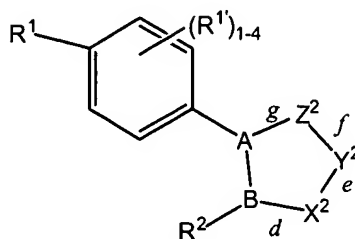


Listing of Claims:

1 - 58 (Cancelled)

59. (Previously Amended) A compound of Formula (II), or a pharmaceutically acceptable salt thereof;



II

wherein:

A-B is:

- (a) N-C;
- (b) C-N; or
- (c) N-N;

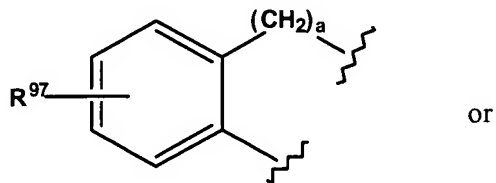
when sides *d* and *f* are double bonds, and sides *e* and *g* are single bonds,

-X²-Y²-Z²- is:

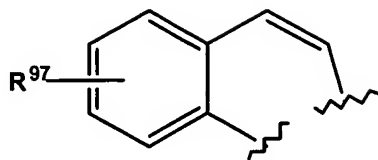
- (a) =CR⁴-CR⁴¹=CR⁵-;
- (b) =CR⁴-CR⁵=N-; or
- (c) =CR²'-CR⁵=N-;

R² and R²', as defined herein taken together are:

- (a)



(b)



or $R^{2'}$ and R^5 , as defined herein, taken together with the carbon atoms to which they are attached are a cycloalkyl group or a heterocyclic ring;

R^{97} is:

- (a) hydrogen;
- (b) alkylthio;
- (c) alkylsulfinyl;
- (d) alkylsulfonyl;
- (e) cyano;
- (f) carboxyl;
- (g) amino;
- (h) lower alkyl;
- (i) haloalkyl;
- (j) hydroxy;
- (k) alkoxy;
- (l) haloalkoxy;
- (m) alkylarylalkylamino;
- (n) aminoalkyl;
- (o) aminoaryl;
- (p) sulfonamido;
- (q) alkylsulfonamido;
- (r) arylsulfonamido;
- (s) heterocyclic ring;
- (t) hydroxyalkyl; or
- (u) nitro;

a is an integer from 1 to 3;

when sides e and g are double bonds, and sides d and f are single bonds,

$-X^2-Y^2-Z^2-$ is:

(a) $-N=CR^4-CR^5=$; or

(b) $-CR^4=CR^5-CR^5=$;

R^1 is:

(a) $-S(O)_2-CH_3$;

(b) $-S(O)_2-NR^8(D^1)$; or

(c) $-S(O)(NH)CH_3$;

$R^{1'}$ at each occurrence is independently:

(a) hydrogen;

(b) halogen;

(c) methyl; or

(d) CH_2OH ;

R^2 is:

(a) lower alkyl;

(b) cycloalkyl;

(c) mono-, di- or tri-substituted phenyl or naphthyl, wherein the substituents are

each independently:

(1) hydrogen;

(2) halo;

(3) alkoxy;

(4) alkylthio;

(5) CN ;

(6) haloalkyl, preferably CF_3 ;

(7) lower alkyl;

(8) N_3 ;

(9) $-CO_2D^1$;

(10) $-CO_2$ -lower alkyl;

- (11) $-(C(R^5)(R^6))_z-OD^1$;
- (12) $-(C(R^5)(R^6))_z-O$ -lower alkyl;
- (13) lower alkyl-CO₂-R⁵ ;
- (14) -OD¹;
- (15) haloalkoxy;
- (16) amino;
- (17) nitro;
- (18) alkylsulfinyl; or
- (19) heteroaryl;

(d) mono-, di- or tri-substituted heteroaryl, wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one heteroatom which is S, O, or N, and, optionally, 1, 2, or 3 additional N atoms; or the heteroaryl is a monocyclic ring of 6 atoms, said ring having one heteroatom which is N, and, optionally, 1, 2, 3, or 4 additional N atoms; wherein the substituents are each independently:

- (1) hydrogen;
 - (2) halo;
 - (3) lower alkyl;
 - (4) alkoxy;
 - (5) alkylthio;
 - (6) CN;
 - (7) haloalkyl, preferably CF₃;
 - (8) N₃;
 - (9) $-C(R^5)(R^6)-OD^1$;
 - (10) $-C(R^5)(R^6)-O$ -lower alkyl; or
 - (11) alkylsulfinyl;
- (e) benzoheteroaryl which includes the benzo fused analogs of (d);
- (f) -NR¹⁰ R¹¹;
 - (g) -SR¹¹;
 - (h) -OR¹¹;

(i) $-R^{11}$;

(j) alkenyl;

(k) alkynyl;

(l) unsubstituted, mono-, di-, tri- or tetra-substituted cycloalkenyl, wherein the substituents are each independently:

(1) halo;

(2) alkoxy;

(3) alkylthio;

(4) CN;

(5) haloalkyl, preferably CF_3 ;

(6) lower alkyl;

(7) N_3 ;

(8) $-CO_2D^1$;

(9) $-CO_2$ -lower alkyl;

(10) $-C(R^{12})(R^{13})-OD^1$;

(11) $-C(R^{12})(R^{13})-O$ -lower alkyl;

(12) lower alkyl- CO_2-R^{12} ;

(13) benzyloxy;

(14) $-O$ -(lower alkyl)- CO_2R^{12} ;

(15) $-O$ -(lower alkyl)- $NR^{12}R^{13}$; or

(16) alkylsulfinyl;

(m) mono-, di-, tri- or tetra-substituted heterocycloalkyl group of 5, 6 or 7 members, or a benzoheterocycle, wherein said heterocycloalkyl or benzoheterocycle contains 1 or 2 heteroatoms selected from O, S, or N and, optionally, contains a carbonyl group or a sulfonyl group, and wherein said substituents are each independently:

(1) halo;

(2) lower alkyl;

(3) alkoxy;

(4) alkylthio;

- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) -C(R¹²)(R¹³)-OD¹;
- (9) -C(R¹²)(R¹³)-O-lower alkyl; or
- (10) alkylsulfinyl;

(n) styryl, mono or di-substituted styryl, wherein the substituent are each independently:

- (1) halo;
- (2) alkoxy;
- (3) alkylthio;
- (4) CN;
- (5) haloalkyl, preferably CF₃;
- (6) lower alkyl;
- (7) N₃;
- (8) -CO₂D¹;
- (9) -CO₂-lower alkyl;
- (10) -C(R¹²)(R¹³)-OD¹;
- (11) -C(R¹²)(R¹³)-O-lower alkyl;
- (12) lower alkyl-CO₂-R¹² ;
- (13) benzyloxy;
- (14) -O-(lower alkyl)-CO₂R¹²; or
- (15) -O-(lower alkyl)-NR¹²R¹³ ;

(o) phenylacetylene, mono- or di-substituted phenylacetylene, wherein the substituents are each independently:

- (1) halo;
- (2) alkoxy;
- (3) alkylthio;
- (4) CN;

- (5) haloalkyl, preferably CF_3 ;
- (6) lower alkyl;
- (7) N_3 ;
- (8) $-\text{CO}_2\text{D}^1$;
- (9) $-\text{CO}_2$ -lower alkyl;
- (10) $-\text{C}(\text{R}^{12})(\text{R}^{13})-\text{OD}^1$;
- (11) $-\text{C}(\text{R}^{12})(\text{R}^{13})-\text{O}$ -lower alkyl;
- (12) lower alkyl- $\text{CO}_2-\text{R}^{12}$;
- (13) benzyloxy;
- (14) $-\text{O}$ -(lower alkyl)- CO_2R^{12} ; or
- (15) $-\text{O}$ -(lower alkyl)- $\text{NR}^{12}\text{R}^{13}$;

(p) fluoroalkenyl;

(q) mono- or di-substituted bicyclic heteroaryl of 8, 9 or 10 members, containing 2, 3, 4 or 5 heteroatoms, wherein at least one heteroatom resides on each ring of said bicyclic heteroaryl, said heteroatoms are each independently O, S and N and said substituents are each independently:

- (1) hydrogen;
- (2) halo;
- (3) lower alkyl;
- (4) alkoxy;
- (5) alkylthio;
- (6) CN;
- (7) haloalkyl, preferably CF_3 ;
- (8) N_3 ;
- (9) $-\text{C}(\text{R}^5)(\text{R}^6)-\text{OD}^1$; or
- (10) $-\text{C}(\text{R}^5)(\text{R}^6)-\text{O}$ -lower alkyl;

(r) K;

(s) aryl;

(t) arylalkyl;

- (u) cycloalkylalkyl;
- (v) $-C(O)R^{11}$;
- (u) hydrogen;
- (v) arylalkenyl;
- (w) arylalkoxy;
- (x) alkoxy;
- (y) aryloxy;
- (z) cycloalkoxy;
- (aa) arylthio;
- (bb) alkylthio;
- (cc) arylalkylthio; or
- (dd) cycloalkylthio;

R^4 , $R^{4'}$, R^5 and $R^{5'}$ are each independently:

- (a) hydrogen;
- (b) amino;
- (c) CN;
- (d) lower alkyl;
- (e) haloalkyl;
- (f) alkoxy;
- (g) alkylthio;
- (h) Q;
- (i) $-O-Q$;
- (j) $-S-Q$;
- (k) K;
- (l) cycloalkoxy;
- (m) cycloalkylthio;

(n) unsubstituted, mono-, or di-substituted phenyl or unsubstituted, mono-, or di-substituted benzyl, wherein the substituents are each independently:

- (1) halo;

- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) Q;
- (9) nitro; or
- (10) amino;

(o) unsubstituted, mono-, or di-substituted heteroaryl or unsubstituted, mono-, or di-substituted heteroarylmethyl, wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one heteroatom which is S, O, or N, and, optionally, 1, 2, or 3 additional N atoms; or the heteroaryl is a monocyclic ring of 6 atoms, said ring having one heteroatom which is N, and, optionally, 1, 2, 3, or 4 additional N atoms; said substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) -C(R⁶)(R⁷)-OD¹;
- (9) -C(R⁶)(R⁷)-O-lower alkyl; or
- (10) alkylsulfinyl

(p) -CON(R⁸)(R⁸);

(q) -CH₂OR⁸;

(r) -CH₂OCN;

(s) unsubstituted or substituted:

- (1) lower alkyl-Q;

- (2) -O-lower alkyl-Q;
- (3) -S-lower alkyl-Q;
- (4) lower alkyl-O-lower alkyl-Q;
- (5) lower alkyl-S-lower alkyl-Q;
- (6) lower alkyl-O-Q;
- (7) lower alkyl-S-Q;
- (8) lower alkyl-O-K;
- (9) lower alkyl-S-K;
- (10) lower alkyl-O-V; or
- (11) lower alkyl-S-V;

wherein the substituent(s) resides on the lower alkyl;

- (t) cycloalkyl;
- (u) aryl;
- (v) arylalkyl;
- (w) cycloalkylalkyl;
- (x) aryloxy;
- (y) arylalkoxy;
- (z) arylalkylthio;
- (aa) cycloalkylalkoxy;
- (bb) heterocycloalkyl;
- (cc) alkylsulfonyloxy;
- (dd) alkylsulfonyl;
- (ee) arylsulfonyl;
- (ff) arylsulfonyloxy;
- (gg) -C(O)R¹⁰;
- (hh) nitro;
- (ii) amino;
- (jj) aminoalkyl;
- (kk) -C(O)-alkyl-heterocyclic ring;

- (ll) halo;
- (mm) heterocyclic ring;
- (nn) $\text{-CO}_2\text{D}^1$;
- (oo) carboxyl;
- (pp) amidyl; or
- (qq) alkoxyalkyl;

alternatively, R^4 and R^5 together with the carbons to which they are attached are:

- (a) cycloalkyl;
- (b) aryl; or
- (c) heterocyclic ring;

alternatively, R^4 and $\text{R}^{4'}$ or R^5 and $\text{R}^{5'}$ taken together with the carbon to which they are attached are:

- (a) cycloalkyl; or
- (b) heterocyclic ring;

alternatively, R^4 and R^5 , $\text{R}^{4'}$ and $\text{R}^{5'}$, R^4 and $\text{R}^{5'}$, or $\text{R}^{4'}$ and R^5 when substituents on adjacent carbon atoms taken together with the carbons to which they are attached are:

- (a) cycloalkyl;
- (b) heterocyclic ring; or
- (c) aryl;

R^6 and R^7 are each independently:

- (a) hydrogen;
- (b) unsubstituted, mono- or di-substituted phenyl; unsubstituted, mono- or di-substituted benzyl; unsubstituted, mono- or di-substituted heteroaryl; mono- or di-substituted heteroarylmethyl, wherein said substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;

- (6) haloalkyl, preferably CF_3 ;
- (7) N_3 ;
- (8) $-\text{C}(\text{R}^{14})(\text{R}^{15})-\text{OD}^1$; or
- (9) $-\text{C}(\text{R}^{14})(\text{R}^{15})-\text{O}$ -lower alkyl;

- (c) lower alkyl;
- (d) $-\text{CH}_2\text{OR}^8$;
- (e) CN ;
- (f) $-\text{CH}_2\text{CN}$;
- (g) haloalkyl, preferably fluoroalkyl;
- (h) $-\text{CON}(\text{R}^8)(\text{R}^8)$;
- (i) halo; or
- (j) $-\text{OR}^8$;

R^8 is:

- (a) hydrogen;
- (b) K ; or
- (c) R^9 ;

alternatively, R^5 and $\text{R}^{5'}$, R^6 and R^7 or R^7 and R^8 together with the carbon to which they are attached form a saturated monocyclic ring of 3, 4, 5, 6 or 7 atoms; optionally containing up to two heteroatoms selected from oxygen, $\text{S}(\text{O})_0$ or NR_i ;

R^9 is:

- (a) lower alkyl;
- (b) lower alkyl- CO_2D^1 ;
- (c) lower alkyl- NHD^1 ;
- (d) phenyl or mono-, di- or tri-substituted phenyl, wherein the substituents are

each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;

- (5) lower alkyl-CO₂D¹;
- (6) lower alkyl-NHD¹;
- (7) CN;
- (8) CO₂D¹; or
- (9) haloalkyl, preferably fluoroalkyl;

(e) benzyl, mono-, di- or tri-substituted benzyl, wherein the substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) lower alkyl-CO₂D¹;
- (6) lower alkyl-NHD¹;
- (7) CN;
- (8) -CO₂D¹; or
- (9) haloalkyl, preferably CF₃;

(f) cycloalkyl;

(g) K; or

(h) benzoyl, mono-, di-, or trisubstituted benzoyl, wherein the substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) lower alkyl-CO₂D¹;
- (6) lower alkyl-NHD¹;
- (7) CN;
- (8) -CO₂D¹; or
- (9) haloalkyl, preferably CF₃;

R^{10} and $R^{10'}$ are each independently:

- (a) hydrogen; or
- (b) R^{11} ;

R^{11} is:

- (a) lower alkyl;
- (b) cycloalkyl;
- (c) unsubstituted, mono-, di- or tri-substituted phenyl or naphthyl, wherein the

substituents are each independently:

- (1) halo;
- (2) alkoxy;
- (3) alkylthio;
- (4) CN;
- (5) haloalkyl, preferably CF_3 ;
- (6) lower alkyl;
- (7) N_3 ;
- (8) $-CO_2D^1$;
- (9) $-CO_2$ -lower alkyl;
- (10) $-C(R^{12})(R^{13})-OD^1$;
- (11) $-C(R^{12})(R^{13})-O$ -lower alkyl;
- (12) lower alkyl- CO_2D^1 ;
- (13) lower alkyl- CO_2R^{12} ;
- (14) benzyloxy;
- (15) $-O$ -(lower alkyl)- CO_2D^1 ;
- (16) $-O$ -(lower alkyl)- CO_2R^{12} ; or
- (17) $-O$ -(lower alkyl)- $NR^{12}R^{13}$;

(d) unsubstituted, mono-, di- or tri-substituted heteroaryl, wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one heteroatom which is S, O, or N, and, optionally, 1, 2, or 3 additional N atoms; or said heteroaryl is a monocyclic ring of 6 atoms, said

ring having one heteroatom which is N, and, optionally 1, 2, or 3 additional N atoms, and wherein said substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) -C(R¹²)(R¹³)-OD¹; or
- (9) -C(R¹²)(R¹³)-O-lower alkyl;

(e) unsubstituted, mono- or di-substituted benzoheterocycle, wherein the benzoheterocycle is a 5, 6, or 7-membered ring which contains 1 or 2 heteroatoms independently selected from O, S, or N, and, optionally, a carbonyl group or a sulfonyl group, wherein said substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) -C(R¹²)(R¹³)-OD¹; or
- (9) -C(R¹²)(R¹³)-O-lower alkyl;

(f) unsubstituted, mono- or di-substituted benzocarbocycle, wherein the carbocycle is a 5, 6, or 7-membered ring which optionally contains a carbonyl group, wherein said substituents are each independently :

- (1) halo;
- (2) lower alkyl;

- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) -C(R¹²)(R¹³)-OD¹; or
- (9) -C(R¹²)(R¹³)-O-lower alkyl;

(g) hydrogen; or

(h) K

R¹² and R¹³ are each independently:

- (a) hydrogen;
- (b) lower alkyl; or
- (c) aryl; or

R¹² and R¹³ together with the atom to which they are attached form a saturated monocyclic ring of 3, 4, 5, 6 or 7 atoms;

R¹⁴ and R¹⁵ are each independently :

- (a) hydrogen; or
- (b) lower alkyl; or

R¹⁴ and R¹⁵ together with the atom to which they are attached form a carbonyl, a thial, or a saturated monocyclic ring of 3, 4, 5, 6 or 7 atoms;

D¹ is:

- (a) hydrogen or
- (b) D;

D is:

- (a) V; or
- (b) K;

U is:

- (a) oxygen;
- (b) sulfur; or

(c) $-N(R_a)(R_i)-$;

V is:

(a) $-NO$;

(b) $-NO_2$; or

(c) hydrogen

K is $-W_{aa}-E_b-(C(R_e)(R_f))_p-E_c-(C(R_e)(R_f))_x-W_d-(C(R_e)(R_f))_y-W_i-E_j-W_g-(C(R_e)(R_f))_z-U-V$;

wherein aa, b, c, d, g, i and j are each independently an integer from 0 to 3;

p, x, y and z are each independently an integer from 0 to 10;

W at each occurrence is independently:

(a) $-C(O)-$;

(b) $-C(S)-$;

(c) $-T-$;

(d) $-(C(R_e)(R_f))_h-$;

(e) alkyl;

(f) aryl;

(g) heterocyclic ring;

(h) arylheterocyclic ring, or

(i) $-(CH_2CH_2O)_q-$;

E at each occurrence is independently:

(a) $-T-$;

(b) alkyl;

(c) aryl;

(d) $-(C(R_e)(R_f))_h-$;

(e) heterocyclic ring;

(f) arylheterocyclic ring; or

(g) $-(CH_2CH_2O)_q-$;

h is an integer from 1 to 10;

q is an integer from 1 to 5;

R_e and R_f are each independently:

- (a) hydrogen;
- (b) alkyl;
- (c) cycloalkoxy;
- (d) halogen;
- (e) hydroxy;
- (f) hydroxyalkyl;
- (g) alkoxyalkyl;
- (h) arylheterocyclic ring;
- (i) cycloalkylalkyl;
- (j) heterocyclicalkyl;
- (k) alkoxy;
- (l) haloalkoxy;
- (m) amino;
- (n) alkylamino;
- (o) dialkylamino;
- (p) arylamino;
- (q) diarylamino;
- (r) alkylarylamino;
- (s) alkoxyhaloalkyl;
- (t) haloalkoxy;
- (u) sulfonic acid;
- (v) alkylsulfonic acid;
- (w) arylsulfonic acid;
- (x) arylalkoxy;
- (y) alkylthio;
- (z) arylthio;
- (aa) cyano;
- (bb) aminoalkyl;
- (cc) aminoaryl;

(dd) alkoxy;
(ee) aryl;
(ff) arylalkyl;
(gg) carboxamido;
(hh) alkylcarboxamido;
(ii) arylcarboxamido;
(jj) amidyl;
(kk) carboxyl;
(ll) carbamoyl;
(mm) alkylcarboxylic acid;
(nn) arylcarboxylic acid;
(oo) alkylcarbonyl;
(pp) arylcarbonyl;
(qq) ester;
(rr) carboxylic ester;
(ss) alkylcarboxylic ester;
(tt) arylcarboxylic ester;
(uu) haloalkoxy;
(vv) sulfonamido;
(ww) alkylsulfonamido;
(xx) arylsulfonamido;
(yy) alkylsulfonyl,
(zz) alkylsulfonyloxy,
(aaa) arylsulfonyl,
(bbb) arylsulphonyloxy
(ccc) sulfonic ester;
(ddd) carbamoyl;
(eee) urea;
(fff) nitro;

(ggg) -U-V; or

(hhh) -(C(R'_e)(R'_f))_k-U-V or

R_e and R_f taken together are:

- (a) oxo;
- (b) thial;
- (c) oxime; or
- (d) hydrazone;

R_e and R_f taken together with the carbon atom to which they are attached are:

- (a) heterocyclic ring;
- (b) cycloalkyl group; or
- (c) bridged cycloalkyl group;

R'_e and R'_f are each independently selected from R_e;

k is an integer from 1 to 3;

T at each occurrence is independently:

- (a) a covalent bond,
- (b) carbonyl,
- (c) an oxygen,
- (d) -S(O)_o-; or
- (e) -N(R_a)(R_i)-;

o is an integer from 0 to 2;

Q is:

- (a) -C(O)-U-D¹;
- (b) -CO₂-lower alkyl;
- (c) tetrazolyl-5-yl;
- (d) -C(R⁷)(R⁸)(S-D¹);
- (e) -C(R⁷)(R⁸)(O-D¹); or
- (f) -C(R⁷)(R⁸)(O-lower alkyl);

R_a is:

- (a) a lone pair of electron;

(b) hydrogen; or

(c) lower alkyl;

R_i is:

(a) hydrogen;

(b) alkyl;

(c) aryl;

(d) alkylcarboxylic acid;

(e) arylcarboxylic acid;

(f) alkylcarboxylic ester;

(g) arylcarboxylic ester;

(h) alkylcarboxamido;

(i) arylcarboxamido;

(j) alkylsulfinyl;

(k) alkylsulfonyl;

(l) alkylsulfonyloxy,

(m) arylsulfinyl;

(n) arylsulfonyl;

(o) arylsulphonyloxy;

(p) sulfonamido;

(q) carboxamido;

(r) carboxylic ester;

(s) aminoalkyl;

(t) aminoaryl;

(u) -CH₂-C(U-V)(R_e)(R_f);

(v) a bond to an adjacent atom creating a double bond to that atom; or

(w) -(N₂O₂-)⁻•M⁺, wherein M⁺ is an organic or inorganic cation;

with the proviso that the compound of Formula (II) must contain at least one oxime group and/or hydrazone group.

60. (Previously Presented) A composition comprising the compound of claim 59 and a pharmaceutically acceptable carrier.

61. (Previously Presented) A method for treating or reducing inflammation, pain or fever in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 60.

62. (Previously Presented) A method for treating a gastrointestinal disorder, or improving the gastrointestinal properties of a COX-2 inhibitor in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 60.

63. (Previously Presented) The method of claim 62, wherein the gastrointestinal disorder is an inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, ulcerative colitis, a peptic ulcer, a stress ulcer, a bleeding ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, a bacterial infection, short-bowel (anastomosis) syndrome, or a hypersecretory state associated with systemic mastocytosis or basophilic leukemia and hyperhistaminemia.

64. (Previously Presented) A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 60.

65. (Previously Presented) The method of claim 64, wherein the wound is an ulcer.

66. (Previously Presented) A method for treating or reversing renal and/or respiratory toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 60.

67. (Previously Presented) A method for treating a disorder resulting from elevated levels of COX-2 in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 60.

68. (Previously Presented) The method of claim 67, wherein the disorder resulting from elevated levels of COX-2 is angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, premature labor, tendinitis, bursitis, a skin-related condition, neoplasia, an inflammatory process in a disease, an ophthalmic disorder, pulmonary inflammation, a central nervous system disorder,

allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, a microbial infection, a cardiovascular disorder, a urinary disorder, a urological disorder, endothelial dysfunction, organ deterioration, tissue deterioration, or activation, adhesion and infiltration of neutrophils at the site of inflammation.

69. (Previously Presented) The method of claim 10, wherein the neoplasia is a brain cancer, a bone cancer, an epithelial cell-derived neoplasia (epithelial carcinoma), a basal cell carcinoma, an adenocarcinoma, a gastrointestinal cancer, a lip cancer, a mouth cancer, an esophageal cancer, a small bowel cancer, a stomach cancer, a colon cancer, a liver cancer, a bladder cancer, a pancreas cancer, an ovary cancer, a cervical cancer, a lung cancer, a breast cancer, a skin cancer, a squamous cell cancer, a basal cell cancer, a prostate cancer, a renal cell carcinoma, a cancerous tumor, a growth, a polyp, an adenomatous polyp, a familial adenomatous polyposis or a fibrosis resulting from radiation therapy.

70. (Previously Presented) The method of claim 68, wherein the central nervous system disorder is cortical dementia, Alzheimer's disease, vascular dementia, multi-infarct dementia, pre-senile dementia, alcoholic dementia, senile dementia, or central nervous system damage resulting from stroke, ischemia or trauma.

71. (Previously Presented) A method for inhibiting platelet aggregation in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 60.

72. (Previously Presented) The composition of claim 60, further comprising at least one therapeutic agent.

73. (Previously Presented) The composition of claim 72, wherein the therapeutic agent is a steroid, a nonsteroidal antiinflammatory compound, a 5-lipoxygenase (5-LO) inhibitor, a leukotriene B₄ receptor antagonist, a leukotriene A₄ hydrolase inhibitor, a 5-HT agonist, a 3-hydroxy-3-methylglutaryl coenzyme A inhibitor, a H₂ antagonist, an antineoplastic agent, an antiplatelet agent, a thrombin inhibitor, a thromboxane inhibitor, a decongestant, a diuretic, a sedating or non-sedating anti-histamine, an inducible nitric oxide synthase inhibitor, an opioid, an analgesic, a *Helicobacter pylori* inhibitor, a proton pump inhibitor, an isoprostane inhibitor, or a mixture of two or more thereof.

74. (Previously Presented) The composition of claim 73, wherein the nonsteroidal antiinflammatory compound is acetaminophen, aspirin, diclofenac, ibuprofen, ketoprofen or naproxen.

75. (Previously Presented) A method for treating or reducing inflammation, pain or fever in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 72.

76. (Previously Presented) A method for treating a gastrointestinal disorder, or improving the gastrointestinal properties of a COX-2 inhibitor in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 72.

77. (Previously Presented) The method of claim 76, wherein the gastrointestinal disorder is an inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, ulcerative colitis, a peptic ulcer, a stress ulcer, a bleeding ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, a bacterial infection, short-bowel (anastomosis) syndrome, or a hypersecretory state associated with systemic mastocytosis or basophilic leukemia and hyperhistaminemia.

78. (Previously Presented) A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 72.

79. (Previously Presented) The method of claim 78, wherein the wound is an ulcer.

80. (Previously Presented) A method for treating or reversing renal and/or respiratory toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 72.

81. (Previously Presented) A method for treating a disorder resulting from elevated levels of COX-2 in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 72.

82. (Previously Presented) The method of claim 81, wherein the disorder resulting from elevated levels of COX-2 is angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, premature labor, tendinitis, bursitis, a skin-related condition, neoplasia, an inflammatory process

in a disease, an ophthalmic disorder, pulmonary inflammation, a central nervous system disorder, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, a microbial infection, a cardiovascular disorder, a urinary disorder, a urological disorder, endothelial dysfunction, organ deterioration, tissue deterioration, or activation, adhesion and infiltration of neutrophils at the site of inflammation.

83. (Previously Presented) The method of claim 82, wherein the neoplasia is a brain cancer, a bone cancer, an epithelial cell-derived neoplasia (epithelial carcinoma), a basal cell carcinoma, an adenocarcinoma, a gastrointestinal cancer, a lip cancer, a mouth cancer, an esophageal cancer, a small bowel cancer, a stomach cancer, a colon cancer, a liver cancer, a bladder cancer, a pancreas cancer, an ovary cancer, a cervical cancer, a lung cancer, a breast cancer, a skin cancer, a squamous cell cancer, a basal cell cancer, a prostate cancer, a renal cell carcinoma, a cancerous tumor, a growth, a polyp, an adenomatous polyp, a familial adenomatous polyposis or a fibrosis resulting from radiation therapy.

84. (Previously Presented) The method of claim 82, wherein the central nervous system disorder is cortical dementia, Alzheimer's disease, vascular dementia, multi-infarct dementia, pre-senile dementia, alcoholic dementia, senile dementia, or central nervous system damage resulting from stroke, ischemia or trauma.

85. (Previously Presented) A method for inhibiting platelet aggregation in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 72.

86. (Previously Presented) A composition comprising at least one compound of claim 59 and at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase.

87. (Previously Presented) The composition of claim 86, further comprising a pharmaceutically acceptable carrier.

88. (Previously Presented) The composition of claim 86, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of

endogenous nitric oxide or endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is an S-nitrosothiol.

89. (Previously Presented) The composition of claim 88, wherein the S-nitrosothiol is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-N-acetylpenicillamine, S-nitroso-homocysteine, S-nitroso-cysteine, S-nitroso-glutathione, or S-nitroso-cysteinyl-glycine.

90. (Previously Presented) The composition of claim 88, wherein the S-nitrosothiol is:

- (i) $\text{HS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{SNO}$;
- (ii) $\text{ONS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{R}_e$; or
- (iii) $\text{H}_2\text{N}-\text{CH}(\text{CO}_2\text{H})-(\text{CH}_2)_m-\text{C}(\text{O})\text{NH}-\text{CH}(\text{CH}_2\text{SNO})-\text{C}(\text{O})\text{NH}-\text{CH}_2-\text{CO}_2\text{H}$;

wherein m is an integer from 2 to 20; R_e and R_f are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, a cycloalkylalkyl, a heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylaryl amino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cyano, an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, a carboxamido, an alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfonyl, an arylsulfonyloxy, a urea, a nitro, $-\text{T}-\text{Q}'$ -, or $-(\text{C}(\text{R}_g)(\text{R}_h))_k-\text{T}-\text{Q}'$ or R_e and R_f taken together are an oxo, a methanthial, a heterocyclic ring, a cycloalkyl group, an oxime, a hydrazone or a bridged cycloalkyl group; Q' is $-\text{NO}$ or $-\text{NO}_2$; and T is independently a covalent bond, a carbonyl, an oxygen, $-\text{S}(\text{O})_o$ - or $-\text{N}(\text{R}_a)\text{R}_i$ -, wherein o is an integer from 0 to 2, R_a is a lone pair of electrons, a hydrogen or an alkyl group; R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylsulfinyl, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfinyl, an arylsulfonyloxy, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an aminoalkyl, an aminoaryl, $-\text{CH}_2-\text{C}(\text{T}-\text{Q}')(\text{R}_g)(\text{R}_h)$, or $-(\text{N}_2\text{O}_2)^-\cdot\text{M}^+$, wherein M^+ is an organic or inorganic cation; with the

proviso that when R_i is $-\text{CH}_2-\text{C}(\text{T}-\text{Q}')(\text{R}_g)(\text{R}_h)$ or $-(\text{N}_2\text{O}_2)^+\text{M}^+$; then " $\text{T}-\text{Q}'$ " can be a hydrogen, an alkyl group, an alkoxyalkyl group, an aminoalkyl group, a hydroxy group or an aryl group; and R_g and R_h at each occurrence are independently R_e .

91. (Previously Presented) The composition of claim 86, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, nitrosated L-homoarginine, nitrosylated L-homoarginine), citrulline, ornithine, glutamine, lysine, an arginase inhibitor or a nitric oxide mediator.

92. (Previously Presented) The composition of claim 86, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is:

- (i) a compound that comprises at least one ON-O- or ON-N- group;
- (ii) a compound that comprises at least one $\text{O}_2\text{N}-\text{O}-$, $\text{O}_2\text{N}-\text{N}-$ or $\text{O}_2\text{N}-\text{S}-$ or group;
- (iii) a N-oxo-N-nitrosoamine having the formula: $\text{R}^{1''}\text{R}^{2''}\text{N}-\text{N}(\text{O}-\text{M}^+)-\text{NO}$, wherein $\text{R}^{1''}$ and $\text{R}^{2''}$ are each independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M^+ is an organic or inorganic cation.

93. (Previously Presented) The composition of claim 92, wherein the compound comprising at least one ON-O- or ON-N- group is an ON-O-polypeptide, an ON-N-polypeptide, an ON-O-amino acid, an ON-N-amino acid, an ON-O-sugar, an ON-N-sugar, an ON-O-oligonucleotide, an ON-N-oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-O-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-N-hydrocarbon, an ON-O-heterocyclic compound or an ON-N-heterocyclic compound.

94. (Previously Presented) The composition of claim 92, wherein compound comprising at least one O₂N-O-, O₂N-N- or O₂N-S- group is an O₂N-O-polypeptide, an O₂N-N-polypeptide, an O₂N-S-polypeptide, an O₂N-O-amino acid, O₂N-N-amino acid, O₂N-S-amino acid, an O₂N-O-sugar, an O₂N-N-sugar, O₂N-S-sugar, an O₂N-O-oligonucleotide, an O₂N-N-oligonucleotide, an O₂N-S-oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-O-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-N-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-S-hydrocarbon, an O₂N-O-heterocyclic compound, an O₂N-N-heterocyclic compound or an O₂N-S-heterocyclic compound.

95. (Previously Presented) The composition of claim 86, further comprising at least one therapeutic agent.

96. (Previously Presented) The composition of claim 95, wherein the therapeutic agent is a steroid, a nonsteroidal antiinflammatory compound, a 5-lipoxygenase (5-LO) inhibitor, a leukotriene B₄ receptor antagonist, a leukotriene A₄ hydrolase inhibitor, a 5-HT agonist, a HMG CoA inhibitor, a H₂ antagonist, an antineoplastic agent, an antiplatelet agent, a thrombin inhibitor, a thromboxane inhibitor, a decongestant, a diuretic, a sedating or non-sedating anti-histamine, an inducible nitric oxide synthase inhibitor, an opioid, an analgesic, a *Helicobacter pylori* inhibitor, a proton pump inhibitor, an isoprostane inhibitor, or a mixture of two or more thereof.

97. (Previously Presented) The composition of claim 96, wherein the nonsteroidal antiinflammatory compound is acetaminophen, aspirin, diclofenac, ibuprofen, ketoprofen or naproxen.

98. (Previously Presented) A method for treating or reducing inflammation, pain or fever in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 87 or 95.

99. (Previously Presented) A method for treating a gastrointestinal disorder, or improving the gastrointestinal properties of a COX-2 inhibitor in a patient in need thereof

comprising administering to the patient a therapeutically effective amount of the composition of claim 87 or 95.

100. (Previously Presented) The method of claim 99, wherein the gastrointestinal disorder is an inflammatory bowel disease, Crohn's disease, gastritis, irritable bowel syndrome, ulcerative colitis, a peptic ulcer, a stress ulcer, a bleeding ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison syndrome, gastroesophageal reflux disease, a bacterial infection, short-bowel (anastomosis) syndrome, or a hypersecretory state associated with systemic mastocytosis or basophilic leukemia and hyperhistaminemia.

101. (Previously Presented) A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 87 or 95.

102. (Previously Presented) The method of claim 101, wherein the wound is an ulcer.

103. (Previously Presented) A method for treating or reversing renal and/or respiratory toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 87 or 95.

104. (Previously Presented) A method for treating a disorder resulting from elevated levels of COX-2 in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 87 or 95.

105. (Previously Presented) The method of claim 104, wherein the disorder resulting from elevated levels of COX-2 is angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, premature labor, tendinitis, bursitis, a skin-related condition, neoplasia, an inflammatory process in a disease, an ophthalmic disorder, pulmonary inflammation, a central nervous system disorder, allergic rhinitis, respiratory distress syndrome, endotoxin shock syndrome, atherosclerosis, a microbial infection, a cardiovascular disorder, a urinary disorder, a urological disorder, endothelial dysfunction, organ deterioration, tissue deterioration, or activation, adhesion and infiltration of neutrophils at the site of inflammation.

106. (Previously Presented) The method of claim 105, wherein the neoplasia is a brain cancer, a bone cancer, an epithelial cell-derived neoplasia (epithelial carcinoma), a basal cell carcinoma, an adenocarcinoma, a gastrointestinal cancer, a lip cancer, a mouth cancer, an

esophageal cancer, a small bowel cancer, a stomach cancer, a colon cancer, a liver cancer, a bladder cancer, a pancreas cancer, an ovary cancer, a cervical cancer, a lung cancer, a breast cancer, a skin cancer, a squamous cell cancer, a basal cell cancer, a prostate cancer, a renal cell carcinoma, a cancerous tumor, a growth, a polyp, an adenomatous polyp, a familial adenomatous polyposis or a fibrosis resulting from radiation therapy.

107. (Previously Presented) The method of claim 105, wherein the central nervous system disorder is cortical dementia, Alzheimer's disease, vascular dementia, multi-infarct dementia, pre-senile dementia, alcoholic dementia, senile dementia, or central nervous system damage resulting from stroke, ischemia or trauma.

108. (Previously Presented) A method for inhibiting platelet aggregation in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 87 or 95.

109. (Previously Presented) A kit comprising at least one compound of claim 59.

110. (Previously Presented) The kit of claim 109, further comprising (i) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase; (ii) at least one therapeutic agent; or (iii) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and at least one therapeutic agent.

111. (Previously Presented) The kit of claim 110, wherein the at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase; the at least one therapeutic agent; or the at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and at least one therapeutic agent; are in the form of separate components in the kit.

112. (Previously Presented) A kit comprising the composition of claim 72, 87 or 95.

113. (Previously Presented) A compound selected from the group consisting of :
1-(3-(1-(hydroxyimino)-4-(nitrooxy)butyl)-1-phenylpyrazol-5-yl)-4-(methylsulfonyl)benzene;

1-(1-cyclohexyl-3-(1-(hydroxyimino)-4-(nitroxy)butyl)pyrazol-5-yl)-4-(methylsulfonyl)benzene; 1-(3-(2-aza-2-methoxy-1-(3-(nitrooxy)propyl)vinyl-1-cyclohexylpyrazol-5-yl)-4-(methylsulfonyl)benzene; 4-(3-(1-(hydroxyimino)-5-(nitrooxy)butyl)-4-(4-(methylsulfonyl)phenyl)-pyrazolyl)benzenecarbonitrile; 1-(1-cyclohexyl-3-(1-(hydroximino)-6-(nitrooxy)hexyl)-pyrazol-5-yl)-4-(methylsulfonyl)benzene; *tert*-butyl 2-((1E)-2-{1-cyclohexyl-5-[4-(methylsulfonyl)phenyl]pyrazol-3-yl}-5-(nitrooxy)-1-azapent-1-enyloxy)acetate; or a pharmaceutically acceptable salt thereof.

114. (Previously Presented) A composition comprising at least one compound of claim 113 and a pharmaceutically acceptable carrier.

115. (Previously Presented) The composition of claim 114, further comprising (i) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase; (ii) at least one therapeutic agent; or (iii) at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase and at least one therapeutic agent.

116. (Previously Presented) A kit comprising at least one compound of claim 113.